

Enantioselective Organocatalytic Intramolecular Diels–Alder Reactions. The Asymmetric Synthesis of Solanapyrone D.

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Supporting Information

General Information. Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.¹ Organic solutions were concentrated under reduced pressure on a Buchi rotary evaporator. Chromatographic purification of products was accomplished using forced-flow chromatography on ICN 60 32-64 mesh silica gel 63 according to the method described by Still.² Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60-F plates. Visualization of the developed chromatogram was performed by fluorescence quenching, anisaldehyde stain, or potassium permanganate stain.

¹H and ¹³C spectra were recorded on Bruker AM-400 (400 MHz and 100 MHz, respectively), Bruker DRX-500 (500 MHz and 125 MHz, respectively), Varian Mercury-300 (300 MHz and 75 MHz, respectively), or Varian I-500 (500 MHz and 125 MHz, respectively) instruments, as noted, and are internally referenced to residual protio solvent signals. Data for ¹H are reported with chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling constant (Hz), and assignment. Data for ¹³C are reported with chemical shift. IR spectra were recorded on an ASI React-IR 1000 spectrometer and are reported in terms of frequency of absorption (cm⁻¹). Optical Rotations were recorded on a Jasco P-1010 polarimeter (WI lamp, 589 nm, 25°C). Mass spectra were obtained from the UC Irvine Mass Spectral Facility. Gas Chromatography was performed on Hewlett-Packard 5890A and 6890 Series gas chromatographs equipped with a split-mode capillary injection system and flame ionization detectors using a Bodman ChiralDEX Γ -TA (30 m x 0.25 mm) column,

¹ Perrin, D. D.; Armarego, W.L.F. *Purification of Laboratory Chemicals*; 3rd ed., Pergamon Press, Oxford, 1988.

Bodman Chiraldex β -DM (30 m x 0.25 mm) column or Bodman Chiraldex β -PH (30 m x 0.25 mm) column. HPLC analysis was performed on a Hewlett-Packard 1100 Series HPLC at 254nm using the following Chiralcel columns: OD-H (25 cm) and OD guard (5 cm), AD (25 cm) and AD guard (5 cm).

Preparation of 10-Phenyl-deca-2,7,9-trienal (3):

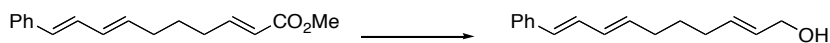


10.0 g (24.10 mmol) of cinnamyltriphenylphosphonium chloride was added to 2.70 g (24.10 mmol) of *t*-BuOK in 100 mL Et₂O and the resulting solution was stirred at room temperature for 30 min. The reaction mixture was cooled to 0°C and 3.42 g (21.91 mmol) of the known aldehyde ester³ was added in 10 mL Et₂O. The solution was warmed to room temperature and stirred for 5 hrs. The solution was poured into 100 mL H₂O and extracted with Et₂O (3 x 50 mL). The combined organics were dried over Na₂SO₄, filtered through cotton, and dried *in vacuo*. The residue was purified by flash chromatography (10% EtOAc/ hexanes) to afford the trienyl ester as a 1:1 mixture of geometric isomers (diene). The mixture was redissolved in 50 mL of CH₂Cl₂ and 250 mg (0.98 mmol) I₂ was added. After 30 min, 20 mL Na₂SO₃ (saturated) were added and the layers were separated. The aqueous layer was extracted (2 x 20 mL) and the combined organics were dried over Na₂SO₃, filtered through cotton, and concentrated *in vacuo* to afford 3.54 g (63%) of trienyl ester as a yellow oil:

IR (film) 3445, 2950, 1722, 1444, 1274, 1205, 1035 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.42-7.17 (m, 5H, PhH), 6.98 (dt, *J* = 7.2, 15.6 Hz, 1H, C₃-H), 6.75 (dd, *J* = 10.5, 15.9 Hz, 1H, C₉-H), 6.45 (d, *J* = 15.6 Hz, 1H, C₁₀-H), 6.21 (dd, *J* = 10.2, 15.0 Hz, 1H, C₈-H), 5.87-5.73 (m, 2H, C₇-H, C₂-H), 3.73 (s, 1H, CO₂CH₃), 2.27-2.14 (m, 4H, C₆-H₂, C₄-H₂), 1.65-1.57 (m, 2H, C₅-H₂); ¹³C NMR (300 MHz, CDCl₃) 167.2, 149.3, 137.7, 134.6, 131.5, 130.7, 129.3, 128.7, 127.4, 126.3, 121.4, 51.8, 32.5, 32.0, 27.9.

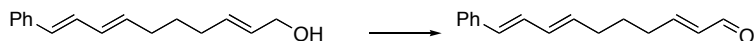
² Still, W.C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923.

³ House, H.O.; Cronin, T.H. *J. Org. Chem.* **1965**, *30*, 1061-1070.



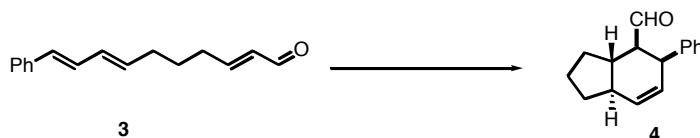
A solution of 1.77 g (6.90 mmol) of trienyl ester in 35 mL CH_2Cl_2 was cooled to -78°C and 2.7 mL (15.19 mmol) of DIBAL-H was added. After one hour, the reaction was allowed to warm to 0°C and 10 mL MeOH was added to quench the remaining DIBAL-H. The slurry was then warmed to room temperature and treated with 50 mL of a solution of saturated aqueous Rochelle's salt. After stirring for 8 hours, the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine (1 x 40 mL), dried over Na_2SO_4 , and concentrated *in vacuo* to afford 1.50 g (95 %) of triene alcohol as a yellow oil which was used in the next reaction without further purification:

IR (film) 3437, 2943, 1715, 1274, 1205, 1027 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.40-7.17 (m, 5H, PhH), 6.75 (dd, $J = 10.4, 15.7$ Hz, 1H, $\text{C}_{10}\text{-H}$), 6.45 (d, $J = 15.7$ Hz, 1H, $\text{C}_{11}\text{-H}$), 6.20 (dd, $J = 10.2, 14.5$ Hz, 1H, $\text{C}_9\text{-H}$), 5.87-5.75 (m, 1H, $\text{C}_8\text{-H}$), 5.70-5.64 (m, 2H, $\text{C}_2\text{-H}$, $\text{C}_3\text{-H}$), 4.09 (m, 2H, $\text{C}_1\text{-H}_2\text{OH}$), 2.17-2.12 (m, 2H, $\text{C}_7\text{-H}_2$), 2.07 (m, 2H, $\text{C}_4\text{-H}_2$), 1.45-1.42 (m, 4H, $\text{C}_5\text{-H}_2$, $\text{C}_6\text{-H}_2$); ^{13}C NMR (300 MHz, CDCl_3) δ 137.7, 135.7, 133.3, 130.1, 129.4, 128.7, 128.6, 127.2, 126.2, 124.4, 64.0, 33.0, 32.3, 29.1, 28.9; ; LRMS (EI) m/z 228; HRMS (EI) exact mass calcd for $[(\text{C}_{16}\text{H}_{20}\text{O})]$ requires m/z 228.1514, found m/z 228.1512.



To a solution of 1.0 g (4.14 mmol) of triene alcohol in 8 mL CH_2Cl_2 was added 970 mg (8.28 mmol) N-methylmorpholine-N-oxide and 100 mg 4A molecular sieves. After 15 minutes, 73 mg (0.21 mmol) of tetrapropylammonium perruthenate was added. After 50 minutes more, the crude reaction mixture was flushed through a 3" silica plug with Et_2O (100 mL) and the eluent was concentrated *in vacuo*. Purification through flash chromatography (10% EtOAc/ Hexanes) afforded 500 mg (50%) of **3** as a yellow oil: IR (film) 3028, 2935, 2827, 2734, 1684 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 9.50 (dd, $J = 2.0, 8.1$ Hz, 1H, C_1HO), 7.39-7.17 (m, 5H, PhH), 6.90-6.71 (m, 2H, $\text{C}_3\text{-H}$, $\text{C}_{10}\text{-H}$), 6.45

(d, $J = 15.9$ Hz, 1H, C₁₁-H), 6.26-6.08 (m, 2H, C₉-H, C₂-H), 5.80 (dt, $J = 6.9, 15.3$ Hz, 1H, C₈-H), 2.39-2.32 (m, 2H, C₄-H₂), 2.18 (dt, $J = 6.9, 6.9$, 2H, C₇-H₂), 1.58-1.44 (m, 4H, C₅-H₂, C₆-H₂); ¹³C NMR (300 MHz, CDCl₃) δ 194.2, 158.8, 137.7, 135.0, 133.3, 131.2, 130.6, 129.3, 128.8, 127.4, 126.3, 32.9, 32.8, 29.1, 27.7; ; LRMS (EI) m/z 226; HRMS (EI) exact mass calcd for [(C₁₈H₂₂O)] requires m/z 226.1358, found m/z 226.1356.

IMDA Reactions of 3.

(3*R*,4*S*,5*R*,6*S*)-Bicyclo[4.3.0]nonene-3-phenyl-4-carbaldehyde 4. *U s i n g* imidazolidinone catalyst **2a**. A solution of catalyst **2** (10 mg, 0.044 mmol) and TFA (3.4 μ L, 0.044 mmol) in 0.44 mL CH₃CN (2% H₂O), cooled to -20° C, was added to 50 mg (0.22 mmol) of **3** (83.3% *E,E*-diene geometry). After stirring for 20 hrs at -20° C, the reaction mixture was warmed to room temperature. The crude reaction mixture was loaded directly onto a silica column and eluted with 10 % EtOAc/ hexanes to afford 35.4 mg (85% yield)⁴ of cycloadduct (**4**) as an >20:1 mixture of *endo:exo* product.⁵ GC analysis of (**4**) showed that it was formed in 93% ee (β -PH, 122 $^{\circ}$ C isotherm with 5 $^{\circ}$ C ramp at 50 min., t_r (major) = 55.80, t_r (minor) = 56.20).

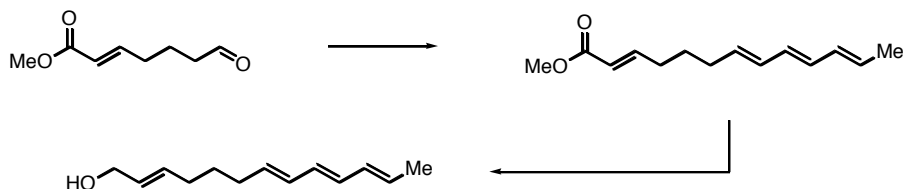
$[\alpha]_D^{25} = 4.35^{\circ}$ ($c = 1$, CHCl₃); IR (film) 2952, 2869, 1719, 1640, 1492, 1452, 913, 744 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 9.05 (d, $J = 4.1$ Hz, 1H, CHO), 7.32-7.18 (m, 5H, PhH), 6.14 (d, $J = 10.1$ Hz, 1H, C₁H), 5.59 (m, 1H, C₂-H), 4.00 (b, 1H, C₃-H), 2.69 (m, 1H, C₄-H), 2.04-1.78 (m, 4H), 1.34-1.25 (m, 3H), 1.08 (m, 1H); ¹³C NMR (300 MHz, CDCl₃) δ 205.1, 151.8, 139.8, 131.0, 129.8, 128.7, 127.3, 57.1, 44.8, 44.2, 39.0, 28.9, 27.6, 22.8; Exact mass calcd for C₁₆H₁₈O (M⁺) 226.1358; found 226.1353 (EI).

(3*R*,4*S*,5*R*,6*S*)-Bicyclo[4.3.0]nonene-3-phenyl-4-carbaldehyde 4. *U s i n g* imidazolidinone catalyst **1a**. A solution of catalyst **1a** (9.5 mg, 0.026 mmol) in 0.27 mL CHCl₃, cooled to $+4^{\circ}$ C, was added to 30 mg (0.133 mmol) of triene **3** (83.3 % *E,E*-diene geometry). After stirring for 23 hr, the reaction mixture was warmed to room temperature. The crude reaction mixture was loaded directly onto a silica column and eluted with 10 % EtOAc/ hexanes to afford 21.0 mg (84% yield)⁴ of cycloadduct **4** as a

⁴ Yield reported based on the conversion of the *E,E*-diene substrate to IMDA product.

>20:1 1:1 mixture of *endo*/ *exo* product.⁶ GC analysis of **4** showed that it was formed in 77% ee. Physical data match those reported above.

Preparation of tetraenal **5**



To a suspension of (2*E*, 4*E*)-hexadiene-1-triphenylphosphonium bromide^{7,8} (1.9 g, 4.6 mmol) in 6.0 mL THF cooled to $-30\text{ }^{\circ}\text{C}$ was added 2.2 mL (4.6 mmol) nBuLi (2.13M in hexanes). The dark red suspension was stirred at $-30\text{ }^{\circ}\text{C}$ for 1 hour, after which 7-oxohept-2-enoic acid methyl ester⁹ (0.65 g, 4.2 mmol) was added in 6.0 mL THF. The solution was warmed to room temperature and stirred for an additional 1.5 hours. The reaction was quenched with H_2O , partitioned, and extracted with hexanes (3 x 30 mL). The organic extracts were combined and washed with brine, dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. The crude ester was taken immediately onto the next step without further purification.

To a solution of crude ester in 42 mL CH_2Cl_2 cooled to $-78\text{ }^{\circ}\text{C}$ was added 1.7 mL (12.6 mmol) of DIBAL-H. The solution was allowed to stir for 15 minutes, after which the reaction was quenched with methanol (5 mL). Upon warming the reaction to room temperature, a saturated solution of sodium potassium tartrate was added (50 mL) and the mixture was stirred vigorously for 8 hours. The mixture was extracted with CH_2Cl_2 (3 x 40 mL), and the combined organic extracts were washed with brine, dried over Na_2SO_4 , and filtered. Volatiles were removed *in vacuo* and the resultant crude oil was purified by silica gel chromatography (1:4 EtOAc/Hexanes) to afford the tetraene alcohol as a clear,

⁵ The epimeric product of the *endo* isomer ((3*R*,4*R*,5*R*,6*S*)-Bicyclo[4.3.0]nonene-3-phenyl-4-carbaldehyde) was present in a ratio of 11:1 *endo:endo* epimer.

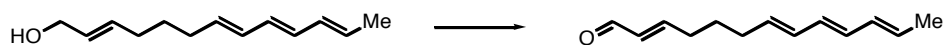
⁶ The epimeric product of the *endo* isomer (4*R*-bicycle) was present in a ratio of 1:1 *endo:endo* epimer.

⁷ *Synthesis* **2000**, 1, 113.

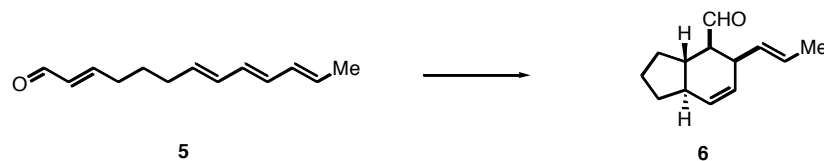
⁸ *J. Am. Chem. Soc.* **1993**, 115, 7653.

⁹ House, H.O.; Cronin, T.H. *J. Org. Chem.* **1965**, 30, 1061.

colorless oil in 63% yield (0.51 g) as a 2.9:1 mixture of (2*E*,7*E*,9*E*,11*E*)- and (2*E*,7*Z*,9*E*,11*E*)- olefin isomers. The mixture was redissolved in 10 mL of CH₂Cl₂ and 50 mg (0.2 mmol) of I₂ was added. After 30 minutes, 10 mL of Na₂S₂O₃ (saturated) were added and the layers were partitioned. The aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL), and the combined organics were washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to provide the title compound as a 5.5:1 (6*E*,8*E*): (6*Z*,8*E*) mixture of geometric isomers in 54% yield (2.1 g). Major isomer: IR (film) 3391, 3012, 2927, 2858, 1668, 1444, 996 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.30-5.99 (m, 4H, CH=CH), 5.75-5.62 (m, 4H, CH=CH), 4.08 (d, *J*=7.1 Hz, 2H, CH₂OH), 2.14-2.00 (m, 4H, CH₂CH=CH, HC=HCCH₂), 1.74 (d, *J*=6.6 Hz, 3H, CH₃CH), 1.49-1.44 (tt, *J*=7.1, 7.1 Hz, 2H, CH₂CH₂CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 133.9, 133.03, 131.9, 131.1, 130.6, 129.4, 129.2, 125.9, 64.1, 32.6, 32.0, 29.0, 18.7; HRMS (EI) exact mass calcd for (C₁₃H₂₀O) requires *m/z* 192.1514, found *m/z* 192.1507.



To a solution of 60 mg (0.31 mmol) of tetraene alcohol in 3 mL of CH₂Cl₂ was added 140 mg (0.33 mmol) of Dess-Martin periodinane and 79 mg (0.90 mmol) of sodium bicarbonate. The solution was stirred at room temperature for 20 minutes, after which 3 mL of 1:1 Na₂S₂O₃/NaHCO₃ aq. solution was added. The aqueous layer was extracted with CH₂Cl₂ (2 x 10 mL), and the combined extracts were washed with brine. The organic extracts were dried over Na₂SO₄, filtered, and concentrated *in vacuo*. Flash chromatography on florisil (10% EtOAc/hexanes) in the absence of light provided the aldehyde **5** as a clear oil in 53% yield (32 mg). Due to compound instability, the aldehyde was used immediately without full characterization. ¹H NMR (300 MHz, CDCl₃) δ 9.50 (d, *J*=7.7 Hz, 1H, CHO), 6.84 (dt, *J*=7.1, 13.2 Hz, 1H, CHCHCHO), 6.22-6.00 (m, 5H, CH=CH), 5.74-5.56 (m, 2H, CH=CH), 2.40-2.28 (m, 2H, CH₂CH=CHCHO), 2.18-2.11 (m, 2H, CH₂CH=CH), 1.76 (d, *J*=5.5 Hz, 3H, CH₃CH), 1.64 (tt, *J*=6.6, 6.6 Hz, 2H, CH₂CH₂CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 194.2, 158.7, 133.3, 132.7, 131.8, 130.6, 130.4, 130.3, 129.6, 32.5, 32.4, 27.8, 18.7.

IMDA reactions of **5**.

(3*R*,4*S*,5*R*,6*S*)-Bicyclo[4.3.0]nonene-3-crotyl-4-carbaldehyde 6. Using imidazolidinone catalyst **1a**. A flask containing tetraene **24** (20 mg, 0.22 mmol, 85% *E,E*-diene geometry) was charged with 0.40 mL of 2% v/v H₂O/CH₃CN and then cooled to –20°C. (5*S*)-5-Benzyl-2,2,3-trimethylimidazolidin-4-one trifluoroacetic acid salt (6.5 mg, 0.02 mmol) was then added in one portion to the solution and the reaction was shaken for 72 hours. The mixture was then loaded onto a silica gel column and eluted with CH₂Cl₂. Removal of volatiles resulted in a oily residue that was purified by silica gel chromatography (5% EtOAc/hexanes) to afford the title compound as a clear oil in 47% yield⁴ (7.8 mg); 4:1 *endo:exo*.¹⁰ *Endo* isomer: IR (film) 3020, 2950, 2873, 1707, 1452, 965 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 9.63 (d, *J*=2.7 Hz, 1H, CHO), 5.88 (d, *J*=9.3, 1H, HC=CH), 5.56-5.29 (m, 3H, HC=CH), 3.36-3.27 (m, 1H, HC=CHCHCH=CH), 2.52 (ddd, *J*=2.7, 6.0, 10.8 Hz, 1H, CHOCH), 2.05-1.95 (m, 1H, CHCHCH₂), 1.89-1.69 (m, 5H, CHCHCH₂, CH₂CH₂CH₂), 1.25-1.01 (m, 2H, CH₂CH₂CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 205.0, 130.1, 130.0, 129.4, 128.5, 56.5, 45.3, 41.6, 39.9, 28.8, 27.8, 22.8, 18.3; HRMS (EI) exact mass calcd for (C₁₃H₁₈O) requires *m/z* 190.1358, found *m/z* 190.1356. [α]_D = +196.2 (*c*=1.0, CHCl₃). Diastereomeric ratios were determined by ¹H NMR analysis. A portion of the title compound was converted to the (2*R*, 4*R*)-pentane-2,4-diol acetal for the determination of enantiomeric purity.¹¹ 5.0 mg of the title compound was taken up in 1 mL of CH₂Cl₂. 4.0 mg of (2*R*, 4*R*)-pentane-2,4-diol and 0.5 mg of pTSA

¹⁰ The epimeric product of the *endo* isomer ((3*R*,4*R*,5*R*,6*S*)-Bicyclo[4.3.0]nonene-3-crotyl-4-carbaldehyde) was observed in this case. The observed ratio of depicted *endo* isomer to *endo* epimer was approximately 2:1. This *endo* epimer was included in the calculation of yield.

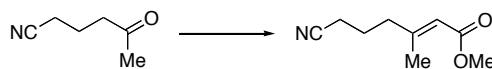
¹¹ The enantiomeric excess of the product was simultaneously determined using the (2*S*, 4*S*)-pentane-2,4-diol to ensure the validity of the assay. Both diols provided identical enantiomeric purity assays.

was added to the solution, and the reaction was stirred for 0.5 hour. NaHCO₃ solution (saturated) was then added, and the mixture was washed with EtOAc (2 x 5 mL). The combined organic extracts were washed with brine, dried over Na₂SO₄, and filtered. The resultant filtrate was loaded onto a short silica plug, eluted with EtOAc, and concentrated, to provide the acetal of the title compound; (*endo*) 87% ee. Enantiomeric excesses were determined by GC with a Chiralex β-DM column (50 °C/10 min, 5 °C/min ramp, 200 °C /20 min); *endo* isomers *t_r*=41.9 min and 42.3 min.

(3*R*,4*S*,5*R*,6*S*)-Bicyclo[4.3.0]nonene-3-crotyl-4-carbaldehyde 6. *Using imidazolidinone catalyst 2a.* A flask containing tetraene **24** (42 mg, 0.22 mmol, 85% *E,E*-diene geometry) was charged with 1.5 mL of 2% v/v H₂O/CH₃CN and then cooled to –20 °C. (2*S*,5*S*)-5-Benzyl-2-*tert*-butyl-3-methylimidazolidin-4-one trifluoroacetic acid salt (11.8 mg, 0.03 mmol) was then added in one portion to the solution and the reaction was shaken for 12 hours. The mixture was then loaded onto a silica gel column and eluted with CH₂Cl₂. Removal of volatiles resulted in a oily residue that was purified by silica gel chromatography (5% EtOAc/hexanes) to afford a compound as a clear oil in 75% yield⁴ (26.7 mg) with spectral data identical to those reported for **6** above; >20:1 *endo:exo*.¹² [α]_D = +212.3 (*c*=1.0, CHCl₃). Diastereomeric ratios were determined by ¹H NMR analysis. A portion of the title compound was converted to the (2*R*, 4*R*)-pentane-2,4-diol acetal for the determination of enantiomeric purity. 5.0 mg of the title compound was taken up in 1 mL of CH₂Cl₂. 4.0 mg of (2*R*, 4*R*)-pentane-2,4-diol and 0.5 mg of pTSA was added to the solution, and the reaction was stirred for 1 hour. NaHCO₃ solution (saturated) was then added, and the mixture was washed with EtOAc (2 x 5 mL). The combined organic extracts were washed with brine, dried over Na₂SO₄, and filtered. The resultant filtrate was loaded onto a short silica plug, eluted with EtOAc, and concentrated, to provide the acetal of the title compound: 94% ee (*endo*).

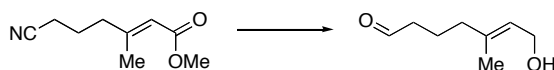
Preparation of 3-Methyl-10-phenyl-deca-2,7,9-trienal (9)

¹² The epimeric product of the *endo* isomer ((4*R*-Bicycle) was present in a ratio of 6:1 *endo:endo* epimer.



170 mL (890 mmol) of methyl diethylphosphonoacetate was added to a solution of 50 mL (439 mmol) of 5-oxohexanenitrile in 1.5 L toluene and the solution was stirred for 10 min. 700 mL NaOMe (prepared from 110.0 g Na and 700 mL MeOH at 0°C) was added to the toluene mixture and the solution was heated to reflux for 2 hrs. The reaction mixture was then cooled to room temperature, poured into 500 mL ice water, and extracted with Et₂O (3 x 300 mL). The combined organic layers were dried over Na₂SO₄, filtered through cotton, and concentrated *in vacuo*. The resulting residue was purified through flash chromatography (20 % EtOAc/ hexanes) to afford 58 g (79%) of the α,β -unsaturated ester as a 1.4: 1 mixture of geometric isomers, which was carried onto to the next step without separation:

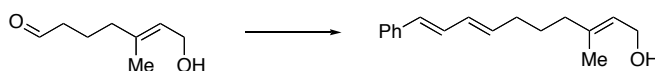
(major-*E*): IR (film) 2950, 1717, 1652, 1436, 1227, 1151 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.53 (m, 1H, C₂-H), 3.49 (s, 3H, CO₂CH₃), 2.21 (t, *J* = 7.1 Hz, 2H, C₆-H₂), 2.12 (t, *J* = 7.1 Hz, 2H, C₄-H₂), 1.98 (d, *J* = 1.1 Hz, 3H, C=C(CH₃)CH₂-), 1.67 (tt, *J* = 7.4, 7.4 Hz, 2H, C₅-H₂); ¹³C NMR (300 MHz, CDCl₃) δ 166.5, 157.2, 119.4, 116.5, 51.0, 39.3, 23.3, 18.5, 16.6; ; LRMS (EI) *m/z* 167; HRMS (EI) exact mass calcd for [(C₉H₁₃NO₂)] requires *m/z* 167.0946, found *m/z* 167.0942.



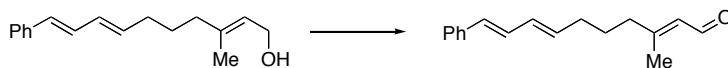
10 g (59.81 mmol) of the nitrile was dissolved in 300 mL CH₂Cl₂ and the reaction mixture was cooled to -78°C. 32.0 mL (179.42 mmol) DIBAL-H was added slowly and the reaction mixture was stirred for 1.5 hrs. 100 mL of MeOH was added to quench the remaining DIBAL-H, then 200 mL of saturated Rochelle's salt solution was added and the resulting slurry was warmed to room temperature and stirred for 12 hrs. The aqueous and organic layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 x 100 mL). The combined organics were washed with brine (200 mL), dried over Na₂SO₄, filtered through cotton, and concentrated *in vacuo*. The resulting residue was purified by

flash chromatography (60-80% EtOAc/ hexanes) to afford 3.67 g (41%) of the aldehyde alcohol as a mixture of isomers:

(major) IR (film) 3385, 2934, 2856, 1717, 999 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 9.72 (m, 1H, CHO), 5.45-5.29 (m, 1H, $\text{C}_6\text{-H}$), 4.08 (dd, $J = 7.0, 14.8$ Hz, $\text{C}_7\text{-H}_2$), 2.43-2.37 (m, 2H, $\text{C}_2\text{-H}_2$), 2.10-1.99 (m, 2H, $\text{C}_4\text{-H}_2$), 1.78-1.68 (m, 2H, $\text{C}_3\text{-H}_2$), 1.62 (s, 3H, $\text{C}=\text{C}(\text{CH}_3)\text{CH}_2\text{-}$); ^{13}C NMR (300 MHz, CDCl_3) δ 202.8, 138.2, 124.7, 59.4, 43.5, 39.0, 23.5, 20.3; ; LRMS (EI) m/z 124 ($[\text{M} - \text{H}_2\text{O}]^+$); HRMS (EI) exact mass calcd for $[(\text{C}_{18}\text{H}_{22}\text{O}) - \text{H}_2\text{O}]^+$ requires m/z 124.0888, found m/z 124.0884.



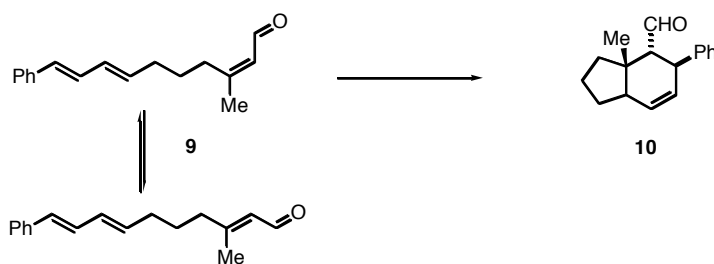
12.85 g (30.97 mmol) of cinnamyltriphenylphosphonium chloride was added to 6.95 g (61.94 mmol) of *t*-BuOK in 130 mL THF and the resulting solution was stirred at room temperature for 30 min. The reaction mixture was cooled to 0°C and 3.67g (25.81 mmol) of the aldehyde was added in 5 mL THF. The solution was warmed to room temperature and stirred for 5 hrs. The reaction mixture was poured into 40 mL H_2O and extracted with Et_2O (3 x 40 mL). The combined organics were dried over Na_2SO_4 , filtered through cotton, and dried *in vacuo*. The residue was purified by flash chromatography (10% EtOAc/ hexanes) to afford the trienyl alcohol as a 1:1 mixture of geometric isomers (diene): IR (film) 3342, 2931, 2860, 1447, 988, 745, 692 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.43-7.17 (m, 5H, PhH), 6.75 (dd, $J = 10.4, 15.6$ Hz, 1H, $\text{C}_9\text{-H}$), 6.45 (d, $J = 15.7$, 1H, $\text{C}_{10}\text{-H}$), 6.26-6.15 (m, 1H, $\text{C}_8\text{-H}$), 5.87-5.77 (m, 1H, $\text{C}_7\text{-H}$), 5.45-5.41 (m, 1H, $\text{C}_2\text{-H}$), 4.15 (m, 2H, $\text{C}_1\text{-H}_2$), 2.17-2.03 (m, 4H, $\text{C}_4\text{-H}_2$, $\text{C}_6\text{-H}_2$), 1.68 (s, 3H, $\text{C}=\text{C}(\text{CH}_3)\text{CH}_2\text{-}$), 1.62-1.48 (m, 2H, $\text{C}_5\text{-H}_2$); ^{13}C NMR (300 MHz, CDCl_3) δ 139.9, 135.5, 131.0, 130.3, 130.3, 129.5, 128.8, 128.7, 127.3, 126.3, 123.7, 59.7, 39.3, 32.7, 27.5, 16.5; LRMS (EI) m/z 242 (M); HRMS (EI) exact mass calcd for $[(\text{C}_{17}\text{H}_{22}\text{O})]$ requires m/z 242.1671, found m/z 242.1679.



To a solution of 1.5 g (6.19 mmol) of trienyl alcohol in 13 mL CH_2Cl_2 was added 1.45 g (12.38 mmol) N-methylmorpholine-N-oxide and 150 mg 4A molecular sieves. After 15 minutes, 109 mg (0.31 mmol) of tetrapropylammonium perruthenate was added. After 15 minutes more, the crude reaction mixture was flushed through a 3" silica plug with Et_2O (200 mL) and the eluent was concentrated to afford **9** as a 1.4:1 mixture of diene isomers. The mixture was redissolved in 20 mL of CH_2Cl_2 and 79 mg (0.31 mmol) I_2 was added. After 20 min, 15 mL Na_2SO_3 (saturated) was added and the layers were separated. The aqueous layer was extracted (2 x 15 mL) and the combined organics were dried over Na_2SO_3 , filtered through cotton, and concentrated *in vacuo*. Purification of the resulting residue (10% EtOAc/ hexanes) afforded 1.20 g (81%) of **9** as a yellow oil:

IR (film): 3028, 2935, 2858, 1668, 1444, 989, 749 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 10.00 (d, $J = 8.1$ Hz, C_1HO), 7.39-7.199 (m, 5H, PhH), 6.74 (dd, $J = 10.8, 15.6$ Hz, 2H, $\text{C}_9\text{-H}$), 6.46 (d, $J = 15.9$ Hz, 1H, $\text{C}_{10}\text{-H}$), 6.22 (dd, $J = 9.0, 15.0$ Hz, 1H, $\text{C}_8\text{-H}$), 5.92-5.87 (m, 1H, $\text{C}_2\text{-H}$), 5.78 (dt, $J = 7.2, 15.0$ Hz, 1H, $\text{C}_7\text{-H}$), 2.26-2.14 (m, 4H, $\text{C}_4\text{-H}_2, \text{C}_6\text{-H}_2$), 2.17 (d, $J = 1.2$ Hz, $\text{C}=\text{C}(\text{CH}_3)\text{CH}_2\text{-}$), 1.70-1.60 (m, 2H, $\text{C}_5\text{-H}_2$); ^{13}C NMR (300 MHz, CDCl_3) δ 191.4, 164.0, 137.6, 134.3, 131.6, 130.8, 129.2, 128.8, 127.6, 127.4, 126.4, 40.3, 32.6, 27.0, 17.9; LRMS (EI) m/z 241 ($[\text{M}]^{++}$); HRMS (EI) exact mass calcd for $[(\text{C}_{17}\text{H}_{20}\text{O})]^+$ requires m/z 240.1514, found m/z 240.1520.

IMDA Reactions of **9**.



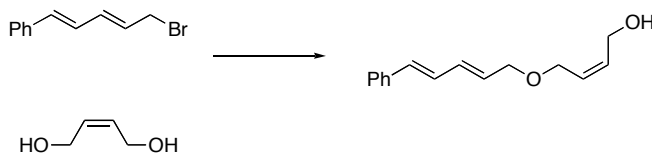
(3R,4S,5R,6S)-Bicyclo[4.3.0]nonene-3-crotyl-5-methyl-4-carbaldehyde 10. Using imidazolidinone catalyst **1b**. To a solution of 6.4 mg (0.025 mmol) of **1b** in 0.25 mL CH_3CN (2 % H_2O) was added 30 mg (83.3 % E,E; 0.125 mmol) of **9**. The solution was stirred at 25°C for 63 hrs, then the crude reaction mixture was flashed through a silica

column and eluted with 10 % EtOAc / hexanes to afford 19.0 mg **10** (76% yield)⁴ as a >20:1 *exo:endo* mixture. The product was subjected to acetalization with chiral *R,R* – pentanediol acetal and the resulting acetal was determined to have 94 % *ee* (GC, DB – 1701, *t_R* (major) 34.74 *t_R* (minor) 35.04).

IR (film) 3024, 2958, 2873, 1716, 750, 702 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 9.96 (d, 1H, *J* = 2.4 Hz, CHO), 7.35-7.16 (m, 5H, PhH), 5.98 (m, 2H, CH=CH), 4.05(m, 1H, CHPh), 2.78(m, 1H, CHCHO), 2.21-1.32 (m, 6H), 0.81(s, 3H, C-CH₃); ¹³C NMR (300 MHz, CDCl₃) δ 203.6, 145.9, 130.2, 129.7, 128.7, 128.1, 126.2, 64.4, 44.4, 43.7, 39.1, 34.1, 25.1, 22.0, 21.5; LRMS (EI) *m/z* 240; HRMS (EI) exact mass calcd for [(C₁₇H₂₀O)] requires *m/z* 240.1514, found *m/z* 240.1509.

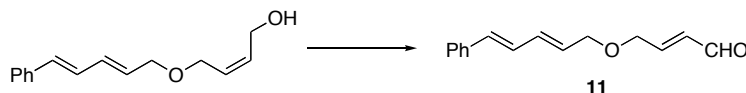
(3*R*,4*S*,5*R*,6*S*)-Bicyclo[4.3.0]nonene-3-crotyl-5-methyl-4-carbaldehyde 10. Using imidazolidinone catalyst **2c**. To a solution of 6.1 mg (0.025 mmol) of **2** and 2.0 μL HClO₄ (0.025 mmol) in 0.25 mL CHCl₃ (2 % H₂O) was added 30 mg (83.3 % E,E; 0.125 mmol) of **9**. The solution was stirred at 4°C for 63 hrs, then the crude reaction mixture was flashed through a silica column and eluted with 10 % EtOAc / hexanes to afford 17.5 mg (70 % yield)⁴ **10** as a 2.5:1 *exo:endo* mixture. The product was subjected to acetalization with chiral *R,R* – pentanediol acetal and the resulting acetal was determined to have 97 % *ee*. Physical data were identical to those reported above.

Preparation of 4-(5-Phenyl-penta-2,4-dienyloxy)-but-2-enal (**11**).



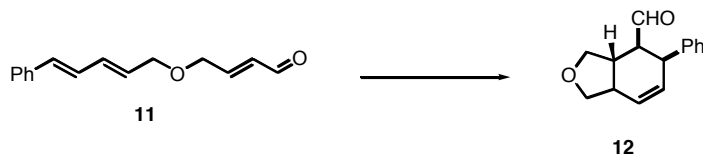
11.6 g (131.65 mmol) of 2-butene-1,4-diol was combined with 354 mg (1.1 mmol) of Bu₄NH₄Br, 15 mL of 50% NaOH (aqueous), and 10 mL CH₂Cl₂. 5.3 g (23.76 mmol) of the dienyyl bromide was added slowly at room temperature and the reaction mixture was stirred for 3 hrs, then poured into 30 mL H₂O. The layers were separated and the aqueous layer was extracted with Et₂O (3 x 70 mL). The combined organic layers were dried over Na₂SO₄,

filtered through cotton, and concentrated *in vacuo*. Purification by flash chromatography (gradient, 20-40% EtOAc/ hexanes) afforded 2.4 g (44%) of the ether alcohol as a yellow oil: IR (film) 3375, 3028, 2866, 1684, 1452, 1027 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.42-7.20 (m, 5H, PhH); 6.78 (dd, $J = 15.6, 10.5$ Hz, 1H, $\text{C}_8\text{-H}$), 6.55 (d, $J = 15.6$ Hz, 1H, $\text{C}_9\text{-H}$), 6.42 (dd, $J = 15.0, 10.5$ Hz, 1H, $\text{C}_7\text{-H}$), 5.93-5.69 (m, 3H, $\text{C}_6\text{-H}$, $\text{C}_3\text{-H}$, $\text{C}_2\text{-H}$), 4.22 (d, $J = 6.0$ Hz, 2H, $\text{C}_1\text{-H}_2$), 4.09 (d, $J = 6.0$ Hz, 4H, $\text{C}_4\text{-H}_2$, $\text{C}_5\text{-H}_2$); ^{13}C NMR (300 MHz, CDCl_3) δ 137.2, 133.6, 133.2, 132.5, 129.7, 128.8, 128.6, 128.2, 127.9, 126.6, 71.0, 65.9, 59.1; LRMS (EI) m/z 230 (M) $^+$; HRMS (EI) exact mass calcd for ($\text{C}_{15}\text{H}_{18}\text{O}_2$) requires m/z 230.1307, found m/z 230.1305.



A solution of 0.21 mL (2.39 mmol) oxalyl chloride in 40 mL CH_2Cl_2 was cooled to -60 $^\circ\text{C}$. 0.34 mL (4.77 mmol) DMSO was added, along with a solution of 500 mg (2.17 mmol) the ether alcohol in 5 mL CH_2Cl_2 . After 15 minutes, 1.5 mL (10.85 mmol) Et_3N was added and the reaction was allowed to warm to room temperature over 40 minutes. The slurry was then poured into 30 mL water, extracted with CH_2Cl_2 (3 x 20 mL), and concentrated *in vacuo*. The product was then run through a basic alumina plug (level IV), eluted with 5 – 10 % EtOAc/ hexanes, concentrated, and used immediately in the IMDA without further purification.

IMDA Reactions of 11.



(3a*S*,4*S*,5*S*,7a*R*)-5-phenyl-1,3,3a,4,5,7a-hexahydro-2-benzofuran-4-carbaldehyde

(12). Using imidazolidinone catalyst **1c**. To a solution of 5.9 mg (0.17 mmol) of **1c** in 0.23 mL *n*BuOH (5 % H_2O) was added 190 mg (0.83 mmol) of **11** in 0.6 mL *n*BuOH.

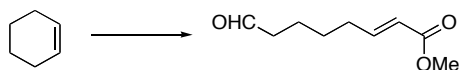
The solution was stirred at -20°C for 6 days, then the crude reaction mixture was warmed to room temperature, flashed through a silica column and eluted with 10 % EtOAc / hexanes to afford 150 mg (79 %) **12** as a >20:1 mixture of *endo:exo* isomers. The product was subjected to acetalization with chiral *R,R* – pentanediol acetal and the resulting acetal was determined to have 94 % *ee*.

$[\alpha]_D^{25} = 284.02^\circ$ ($c = 1$, CHCl_3); IR (film) 2935, 2866, 1722, 1274, 1027, 911 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 9.36(d, 1H, $J = 1.8$ Hz, CHO), 7.34-7.19(m, 5H, PhH), 6.10(d, 1H, $J = 9.6$ Hz, $\text{CH}=\text{CH}$), 5.72(dt, 1H, $J = 3.3, 6.6$ Hz, $\text{CH}=\text{CH}$), 4.24(m, 1H, CHPh), 4.23(t, 1H, $J = 6.9$ Hz, CHHOCH_2), 4.13(t, 1H, $J = 7.2$ Hz, CHHOCH_2), 3.47(dd, 1H, $J = 7.2, 11.4$ Hz, CH_2OCHH), 3.36(dd, 1H, $J = 7.2, 7.4$ Hz, CH_2OCHH), 2.94(ddd, 1H, $J = 1.5, 7.5, 11.4$ Hz, CHCHO), 2.51-2.43 (m, 1H, $-\text{CHCH}_2\text{O}-$), 2.36-2.22(m, 1H, $\text{C}=\text{CHCHCH}_2\text{O}-$); ^{13}C NMR (300 MHz, CDCl_3) δ 201.7, 139.4, 130.8, 129.4, 128.9, 127.7, 125.6, 70.0, 69.9, 54.7, 44.3, 43.6, 39.2.

(3a*S*,4*S*,5*S*,7a*R*)-5-phenyl-1,3,3a,4,5,7a-hexahydro-2-benzofuran-4-carbaldehyde

(12). Using imidazolidinone catalyst **2c**. A solution of 10.8 mg (0.044 mmol) of **2** and 3.8 μL (0.044 mmol) HClO_4 (70 %) in 0.3 mL CH_3CN (2 % H_2O) was added to 50 mg (0.22 mmol) of **11** in 0.1 mL CH_3CN . The solution was stirred at -20°C for 6 days, then the crude reaction mixture was warmed to room temperature, flashed through a silica column and eluted with 10 - 35 % EtOAc / hexanes to afford 42 mg (84 %) **12** as a >20:1 mixture of *endo:exo* isomers.¹³ The product was subjected to acetalization with chiral *R,R* – pentanediol acetal and the resulting acetal was determined to have 93% *ee*. Physical data match those reported above.

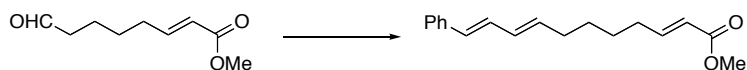
Preparation of 11-Phenyl-undeca-2,8,10-trienal (13).



¹³ The 4-epimeric product of the *endo* isomer ((3a*S*,4*R*,5*S*,7a*R*)-5-phenyl-1,3,3a,4,5,7a-hexahydro-2-benzofuran-4-carbaldehyde) was present in a ratio of 6:1 *endo:endo* epimer.

25.0 g (304.9 mmol) of cyclohexene was dissolved in 120 mL of CH_2Cl_2 and O_3 was bubbled through the solution at -78°C for 11 hrs. 80 g (304.9 mmol) of PPh_3 was added and the reaction mixture was allowed to warm to room temperature and stirred for 8 hrs. 30.5 g (91.2 mmol) of methyl (triphenylphosphoranylidene)acetate was added and the resulting reaction mixture was stirred for 12 hrs longer. Solvent was then removed *in vacuo* and the resulting solid was triturated with Et_2O (3 x 150 mL). The organic liquors were combined and concentrated *in vacuo* and the resulting residue was purified by flash chromatography (20 % EtOAc / hexanes) to afford 8.57 g (55 %) of the aldehyde ester as a pale yellow oil:

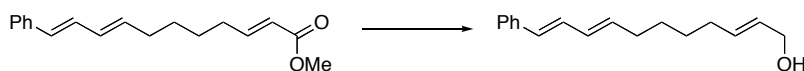
IR (film) 2943, 2866, 2726, 1722, 1661, 1437, 1274, 1205, 1035 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 9.75 (t, $J = 1.5$ Hz, 1H, $\text{C}_8\text{-H}$), 6.93 (dt, $J = 6.9, 15.9$ Hz, 1H, $\text{C}_3\text{-H}$), 5.82 (dt, $J = 1.6, 15.6$ Hz, 1H, $\text{C}_2\text{-H}$), 3.71 (s, 3H, $-\text{CO}_2\text{CH}_3$), 2.45 (dt, $J = 1.5, 7.2$ Hz, 2H, C_7H_2), 2.22 (ddt, $J = 1.5, 7.5, 7.5$ Hz, 2H, $\text{C}_4\text{-H}_2$), 1.70-1.59 (m, 2H, $\text{C}_6\text{-H}_2$), 1.54-1.44 (m, 2H, $\text{C}_5\text{-H}_2$); ^{13}C NMR (300 MHz, CDCl_3) 202.2, 167.1, 148.8, 121.5, 51.8, 43.9, 32.2, 27.8, 21.8; LRMS (EI) m/z 142 ($\text{M}-\text{CO}^+$); HRMS (EI) exact mass calcd for $[(\text{C}_9\text{H}_{14}\text{O}_3) - \text{CO}^+]$ requires m/z 142.0994, found m/z 142.0997.



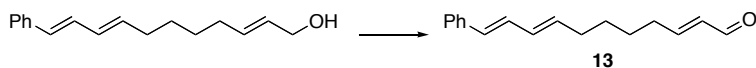
5.46 g (13.16 mmol) of cinnamyltriphenylphosphonium chloride was added to 1.47 g (13.10 mmol) of *t*-BuOK in 45 mL Et_2O and the resulting solution was stirred at room temperature for 30 min. The reaction mixture was cooled to 0°C and 1.72 g (10.11 mmol) of the aldehyde ester was added in 3 mL Et_2O . The solution was warmed to room temperature and stirred for 5 hrs. The solution was poured into 30 mL H_2O and extracted with Et_2O (3 x 25 mL). The combined organics were dried over Na_2SO_4 , filtered through cotton, and dried *in vacuo*. The residue was purified by flash chromatography (10% EtOAc / hexanes) to afford the trienyl ester as a 1:1 mixture of geometric isomers (diene). The mixture was redissolved in 30 mL of CH_2Cl_2 and 167 mg (0.66 mmol) I_2 was added to isomerizes the diene to the desired (*E,E*) geometry. After 30 min, 15 mL Na_2SO_3 (saturated) were added and the layers were separated. The aqueous layer was extracted

(2 x 20 mL) and the combined organics were dried over Na₂SO₃, filtered through cotton, and concentrated *in vacuo* to afford 1.42 g (5.26 mmol) of the trienyl ester as a yellow oil:

IR (film) 3028, 2935, 2858, 1722, 1653, 1437, 1274, 1197, 989 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.45-7.17 (m, 5H, PhH), 6.98 (dt, *J* = 6.9, 15.6 Hz, 1H, C₃-H), 6.75 (dd, *J* = 10.5, 15.6 Hz, 1H, C₁₀-H), 6.45 (d, *J* = 15.6 Hz, 1H, C₁₁-H), 6.20 (dd, *J* = 10.2, 15.0 Hz, 1H, C₉-H), 5.87-5.75 (m, 2H, C₈-H, C₂-H), 3.73 (s, 1H, CO₂CH₃), 2.24-2.13 (m, 4H, C₇-H₂, C₄-H₂), 1.53-1.44 (m, 4H, C₆-H₂, C₅-H₂); ¹³C NMR (300 MHz, CDCl₃) 167.3, 149.6, 137.7, 135.3, 131.1, 130.4, 129.4, 128.7, 127.3, 126.3, 121.2, 51.8, 32.9, 32.4, 29.1, 27.9; LRMS (CI) *m/z* 270 (M)⁺; HRMS (CI) exact mass calcd for (C₁₈H₂₂O₂) requires *m/z* 270.1620, found *m/z* 270.1620.

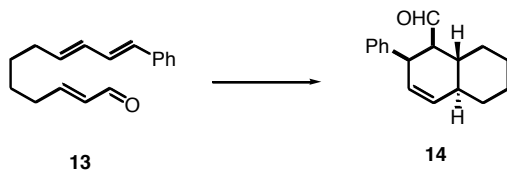


A solution of 2.1 g (7.77 mmol) of the trienyl ester in 77 mL CH₂Cl₂ was cooled to -78°C and 3.0 mL (17.09 mmol) of DIBAL-H was added. After one hour, the reaction was allowed to warm to 0°C and 10 mL MeOH was added to quench the remaining DIBAL-H. The slurry was then warmed to room temperature and treated with 50 mL of a solution of saturated aqueous Rochelle's salt. After stirring for 8 hours, the layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 x 20 mL). The combined organic layers were washed with brine (1 x 40 mL), dried over Na₂SO₄, and concentrated *in vacuo* to afford 1.88 g (100 %) of the trienyl alcohol as a yellow oil which was used in the next reaction without further purification: IR (film) 3355, 2926, 2854, 1448, 987, 745, 691 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.43-7.17 (m, 5H, PhH), 6.75 (dd, *J* = 10.4, 15.7 Hz, 1H, C₁₀-H), 6.45 (d, *J* = 15.7 Hz, 1H, C₁₁-H), 6.20 (dd, *J* = 10.2, 14.5 Hz, 1H, C₉-H), 5.87-5.75 (m, 1H, C₈-H), 5.70-5.64 (m, 2H, C₂-H, C₃-H), 4.09 (m, 2H, C₁-H₂OH), 2.17-2.12 (m, 2H, C₇-H₂), 2.07 (m, 2H, C₄-H₂), 1.45-1.42 (m, 4H, C₅-H₂, C₆-H₂); ¹³C NMR (300 MHz, CDCl₃) δ 137.7, 135.7, 133.3, 130.1, 129.4, 128.7, 128.6, 127.2, 126.2, 124.4, 64.0, 33.0, 32.3, 29.1, 28.9; ; LRMS (EI) *m/z* 242; HRMS (EI) exact mass calcd for [(C₁₇H₂₂O)] requires *m/z* 242.1671, found *m/z* 242.1668.



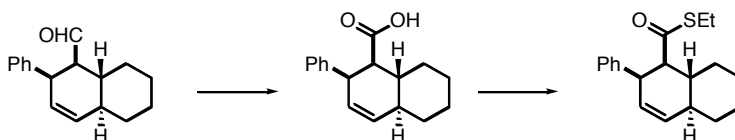
To a solution of 1.0 g (4.14 mmol) of trienyl alcohol in 8 mL CH_2Cl_2 was added 970 mg (8.28 mmol) N-methylmorpholine-N-oxide and 100 mg 4A molecular sieves. After 15 minutes, 73 mg (0.21 mmol) of tetrapropylammonium perruthenate was added. After 50 minutes more, the crude reaction mixture was flushed through a 3'' silica plug with Et_2O (100 mL) and the eluent was concentrated *in vacuo*. Purification through flash chromatography (10% EtOAc/ Hexanes) afforded 500 mg (50%) of **13** as a yellow oil: IR (film): 3014, 2918, 2850, 1688, 1635, 989 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 9.50 (dd, $J = 2.0, 8.1$ Hz, 1H, C_1HO), 7.39-7.17 (m, 5H, PhH), 6.90-6.71 (m, 2H, $\text{C}_3\text{-H}$, $\text{C}_{10}\text{-H}$), 6.45 (d, $J = 15.9$ Hz, 1H, $\text{C}_{11}\text{-H}$), 6.26-6.08 (m, 2H, $\text{C}_9\text{-H}$, $\text{C}_2\text{-H}$), 5.80 (dt, $J = 6.9, 15.3$ Hz, 1H, $\text{C}_8\text{-H}$), 2.39-2.32 (m, 2H, $\text{C}_4\text{-H}_2$), 2.18 (dt, $J = 6.9, 6.9$, 2H, $\text{C}_7\text{-H}_2$), 1.58-1.44 (m, 4H, $\text{C}_5\text{-H}_2$, $\text{C}_6\text{-H}_2$); ^{13}C NMR (300 MHz, CDCl_3) δ 194.2, 158.8, 137.7, 135.0, 133.3, 131.2, 130.6, 129.3, 128.8, 127.4, 126.3, 32.9, 32.8, 29.1, 27.7; ; LRMS (EI) m/z 240; HRMS (EI) exact mass calcd for $[(\text{C}_{17}\text{H}_{20}\text{O})]$ requires m/z 240.1514, found m/z 240.1510.

IMDA Reactions of **13**.



(3R,4S,5R,6S)-Bicyclo[4.4.0]decene-3-phenyl-4-carbaldehyde 14. Using imidazolidinone catalyst **2c**. A flask containing triene **13** (188.8 mg, 0.78 mmol, 80% *E,E*-diene geometry) was charged with 7.8 mL of 2% v/v $\text{H}_2\text{O}/\text{CH}_3\text{CN}$ and then cooled to 4 °C. (2*R*,5*R*)-5-Benzyl-2-*tert*-butyl-3-methylimidazolidin-4-one trifluoromethanesulfonic acid salt (38.5 mg, 0.15 mmol) was then added in one portion to the solution and the reaction was shaken for 16 hours. The mixture was then loaded onto a silica gel column and slowly eluted with 5% EtOAc/Hexanes. Fractions containing

product were combined and concentrated, providing the title compound as a clear oil in 70% yield⁴ (106 mg); *endo:exo* >20:1.¹⁴ *Endo* isomer: IR (film) 3028, 2927, 2858, 1715, 1452 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 8.90 (d, *J*=5.5 Hz, 1H, CHO), 7.35-7.12 (m, 5H, PhH), 5.76 (d, *J*=9.6 Hz, 1H, CH=CH), 5.61 (m, 1H, CH=CH), 3.83 (m, 1H, CHPh), 2.48 (m, 1H, CHCHO), 1.92-0.92 (m, 10H, CH₂CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 207.4, 138.9, 133.4, 130.1, 128.6, 127.3, 127.0, 56.2, 43.6, 41.9, 35.2, 33.4, 30.6, 27.0, 26.7; HRMS (EI) exact mass calcd for (C₁₇H₂₀O) requires *m/z* 240.1514, found *m/z* 240.1517; [α]_D = +626.3 (*c*=1.0, CHCl₃). Diastereomeric ratios were determined by ¹H NMR analysis. A portion of the title compound was reduced to the corresponding primary alcohol for the determination of enantiomeric purity. To a solution of the title compound in absolute ethanol (1 mL) was added 3 equivalents of NaBH₄. After 0.5 hours, the reaction mixture was quenched with H₂O and extracted with 2 x 10 mL CH₂Cl₂. The organic layer was dried over Na₂SO₄, filtered, and concentrated. Purification of the resultant residue by silica gel chromatography provided the corresponding primary alcohol: *endo* 92% ee. ¹H NMR (300 MHz, CDCl₃) δ 7.35-7.19 (m, 5H, PhH), 5.68 (d, *J*=9.9 Hz, 1H, CH=CH), 5.61 (ddd, *J*=2.1, 3.9, 9.9 Hz, 1H, CH=CH), 3.75-3.64 (m, 2H, CH₂OH), 3.34 (m, 1H, CHPh), 1.98-0.86 (m, 11H, CHCH₂OH, CHCH₂, CH₂CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 141.5, 133.4, 130.3, 128.7, 128.6, 128.4, 128.3, 126.9, 62.6, 45.8, 44.63, 43.7, 37.0, 33.7, 29.6, 27.1, 27.0. Enantiomeric ratios were determined by HPLC with a Chiralcel AD column and AD guard column (5% EtOH/hex); *endo* isomers, *t*_r = 11.1 min, 13.4 min.



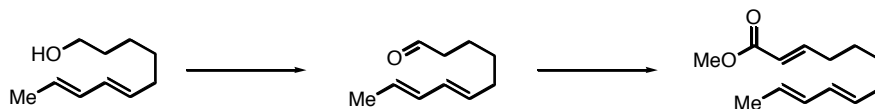
Proof of absolute stereochemistry of (3R,4S,5R,6S)-Bicyclo[4.4.0]decene-3-phenyl-4-carbaldehyde. S-Ethyl-(3R,4S,5R,6S)-Bicyclo[4.4.0]decene-3-phenyl-4-carbothioate 47. 32.1 mg (0.17 mmol) of **14** was dissolved in *tert*-butanol (2.9 mL). To this solution

¹⁴ The 4-epimeric product of the *endo* isomer ((3R,4R,5R,6S)-Bicyclo[4.4.0]decene-3-phenyl-4-carbaldehyde) was present in a ratio of 8:1 *endo:endo* epimer.

was added 2-methyl-2-butene (0.8 mL) and dropwise, a solution of NaClO₂ (139 mg, 1.5 mmol) and NaH₂PO₄ (162 mg, 1.2 mmol) in H₂O (1.6 mL). The biphasic solution was stirred for 12 hours. The reaction was then concentrated, diluted with H₂O, and washed with hexanes. The aqueous layer was acidified with 1N HCl to pH 2, and extracted with Et₂O. The combined organic layers were washed with cold H₂O, dried over Na₂SO₄, filtered, and concentrated to provide the corresponding carboxylic acid: ¹H NMR (300 MHz, CDCl₃) δ 7.44-7.12 (m, 5H, ArH), 5.71 (d, *J*=9.9 Hz, 1H, HC=CH), 5.60 (ddd *J*=2.4, 3.9, 9.9 Hz, 1H HC=CH), 3.81-3.74 (m, 1H, CHPh), 2.78 (dd, *J*=6.6, 12.0 Hz, 1H, CHCOOH), 2.20-1.15 (m, 10H, CH₂CH₂ and CHCH₂); ¹³C NMR (125 MHz, CDCl₃) δ 178.8, 140.2, 133.1, 129.5, 128.1, 127.2, 126.7, 51.3, 44.4, 41.9, 36.0, 32.9, 30.4, 27.2, 26.7.

To acid **46** was added 1 mL CH₂Cl₂, 4-dimethylamino-pyridine (1.2 mg, 0.01 mmol), ethanethiol (9 μL, 0.12 mmol) and dicyclohexylcarbodiimide (24.8 mg, 0.12 mmol). The reaction was stirred for 3 hours, after which time the mixture was filtered and 1N HCl solution (1 mL) was added to resulting filtrate. The layers were partitioned, and the aqueous extracts were washed with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated. The resulting oily residue was purified by silica gel flash chromatography (5% EtOAc/hexanes) to afford compound in 71% yield (21 mg) with spectral data identical to those reported for *S*-Ethyl-(3*R*,4*S*,5*R*,6*S*)-Bicyclo[4.4.0]decene-3-phenyl-4-carbothioate:¹⁵ [α]_D (literature) = -290 (*c*=0.7, CHCl₃), [α]_D = -437 (*c*=1, CHCl₃).

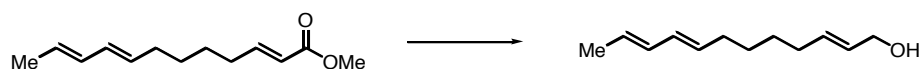
Synthesis of Solanapyrone D.



¹⁵ Evans, D.A.; Johnson, J.S. *J. Am. Chem. Soc.* **1997**, 62, 786.

To a solution of (6*E*,8*E*)-decadienol¹⁶ (1.7g, 11.0 mmol) in CH₂Cl₂ (55mL) was added *N*-methyl morpholine (2.6 g, 22.0 mmol), followed by 300mg of 4Å molecular sieves. After stirring for 20 minutes, tetrapropylammonium perruthenate (77 mg, 0.22 mmol) was added to the mixture. The reaction was worked up after an additional 30 minutes by loading the black colored mixture onto a silica column and eluting with CH₂Cl₂. Most of the solvent was removed *in vacuo* over an ice bath; due to the volatility of the aldehyde, the solution was not concentrated to dryness, and was immediately taken on to the next step.

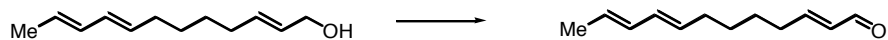
The flask containing (6*E*,8*E*)-decadienal was charged with 20mL of THF, then treated with 3.8 g (10.6 mmol) of methyl (triphenylphosphoranylidene)acetate. The mixture was stirred for 12 hours, after which volatiles were removed *in vacuo*. The resulting solid was triturated with diethyl ether (3 x 100mL), filtered, and the filtrate concentrated. The resulting crude yellow oily residue was purified by silica gel chromatography (5% EtOAc/Hexanes) to afford the title compound as an oil in 52% yield over 2 steps (1.19 g): IR (film) 3020, 2935, 2858, 1722, 1661, 1437, 1274, 1197; ¹H NMR (500 MHz, CDCl₃) δ 7.01-6.94 (m, 1H, CHCHCO₂Me), 6.06-6.01 (m, 2H, CH=CH), 5.83 (d, *J*= 9.3 Hz, 1H, CO₂MeCH), 5.65-5.51 (m, 2H, CHCH₂CHCH₃), 3.72 (s, 3H, OCH₃), 2.25-2.18 (m, 2H, MeO₂CCHCH₂), 2.12-2.07 (m, 2H, CHCH₂), 1.73 (d, *J*=9.0 Hz, 3H, CHCH₃), 1.52-1.40 (m, 4H, CH₂CH₂, CH₂CH₂); ¹³C NMR (125 MHz, CDCl₃) δ 167.4, 149.8, 131.8, 130.9, 129.6, 129.1, 121.2, 51.6, 32.8, 32.5, 32.3, 29.1, 27.8; HRMS (FAB+) exact mass calculated for (MH)⁺ requires *m/z* 209.1542, found *m/z* 209.1541.



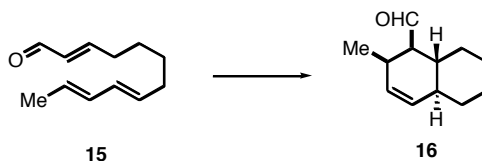
To a solution of # (1.08 g, 5.2 mmol) in 50 mL CH₂Cl₂ cooled to -78 °C was added 2.2 mL (12.6 mmol) of DIBAL-H. The solution was allowed to stir for 15 minutes, after which the reaction was quenched with methanol (5 mL). Upon warming the reaction to room temperature, a saturated solution of sodium potassium tartrate was added (50 mL) and the mixture was stirred vigorously for 8 hours. The mixture was

¹⁶ Oikawa, H.; Kobayashi, T.; Katayama, K.; Suzuki, Y.; Ichihara, A. *J. Org. Chem.* **1998**, 63, 8748.

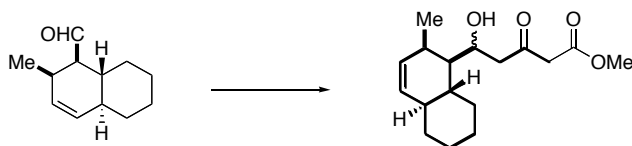
extracted with CH₂Cl₂ (3 x 40 mL), and the combined organic extracts were washed with brine, dried over Na₂SO₄, and filtered. Volatiles were removed *in vacuo* and the resultant crude oil was purified by silica gel chromatography (1:5 EtOAc/Hexanes) to afford the title compound as a clear, colorless oil in 91% yield (0.98 g): IR (film) 3344, 3020, 2927, 2858, 1444, 988 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.01-5.93 (m, 2H, CH=CH), 5.70-5.63 (m, 2H, CH=CH), 5.62-5.48 (m, 2H, CH=CH), 4.06 (d, *J*=9.2 Hz, 2H, CH₂OH), 2.11-2.00 (m, 4H, CHCH₂, CHCH₂), 1.72 (d, *J*=6.0 Hz, 3H, CH₃CH), 1.46-1.33 (m, 4H, CH₂CH₂, CH₂CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 133.4, 131.9, 131.8, 130.6, 129.1, 127.1, 64.1, 32.7, 32.4, 29.3, 29.0, 18.4; HRMS (EI) exact mass calcd for [(C₁₂H₂₀O)] requires *m/z* 180.1514, found *m/z* 180.1519.



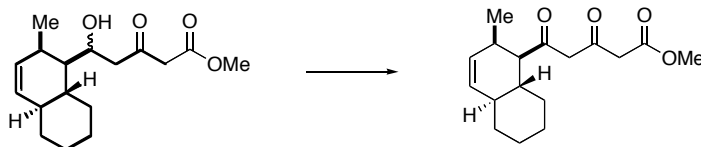
To a solution of # (75 mg, 0.42 mmol) in CH₂Cl₂ (2 mL) was added *N*-methylmorpholine (97 mg, 0.83 mmol), followed by 25 mg of 4Å molecular sieves. After stirring for 20 minutes, tetrapropylammonium perruthenate (3.0 mg, 0.0080 mmol) was added to the mixture. The reaction was worked up after an additional 30 minutes by loading the black colored mixture onto a silica column and eluting with CH₂Cl₂. Removal of volatiles provided a clear crude oily residue which was purified through silica gel chromatography to afford the title compound as a clear oil in 59% yield (44 mg): IR (film) 3020, 2927, 2858, 2734, 1692, 1444, 1120, 980 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 9.47 (d, *J*=8.2 Hz, 1H, CHO), 6.92 (dt, *J*=7.1, 15.4 Hz, 1H, CHCHCHO), 6.07 (dd, *J*=7.8, 15.6 Hz, 1H, CHCHO), 6.00-5.90 (m, 2H, CH=CH, CH=CH), 5.63-5.44 (m, 2H, CH₂CH, CH₃CH), 2.36-2.27 (m, 2H, CH₂CHCHCHO), 2.17-2.01 (d, *J*=6.0 Hz, 3H, CH₃CH), 1.70 (d, *J*=6.0 Hz, 3H, CH₃CH), 1.54-1.37 (m, 4H, CH₂CH₂, CH₂CH₂); ¹³C NMR (75 MHz, CDCl₃) δ 194.2, 158.9, 133.2, 131.6, 131.2, 131.0, 127.4, 32.9, 32.5, 29.2, 27.6, 18.4; HRMS (EI) exact mass calcd for (C₁₂H₁₈O) requires *m/z* 178.1358, found *m/z* 178.1351.



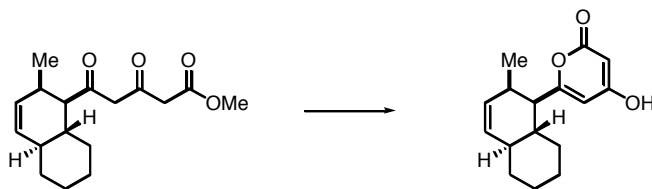
(3*R*,4*S*,5*R*,6*S*)-Bicyclo[4.4.0]decene-3-methyl-4-carbaldehyde 16. A flask containing triene **15** (43.7 mg, 0.25 mmol, 84% *E,E*-diene geometry) was charged with 0.83 mL of 2% v/v H₂O/CH₃CN and then cooled to −5 °C. (2*R*,5*R*)-5-Benzyl-2-*tert*-butyl-3-methylimidazolidin-4-one trifluoromethanesulfonic acid salt (19.4 mg, 0.050 mmol) was then added in one portion to the solution and the reaction was shaken for 48 hours. The mixture was then loaded onto a silica gel column and slowly eluted with 5% EtOAc/Hexanes. Fractions containing product were combined and concentrated, providing the title compound as a clear oil in 71% yield⁴ (26.1 mg); >20:1 *endo:exo* isomer: IR (film) 2927, 1715, 1452, 1267 cm^{−1}; ¹H NMR (300 MHz, CDCl₃) δ 9.73 (d, *J*=4.4 Hz, 1H, CHO), 5.53 (ddd, *J*=2.1, 4.5, 9.9 Hz, 1H, CH=CHCH), 5.40 (d, 9.9 Hz, 1H, CH=CHCH), 2.61-2.55 (m, 1H, CHCH₃), 2.37 (ddd, *J*=4.5, 6.3, 11.1 Hz, 1H, CHCHO), 1.82-1.58 (m, 6H, CHCHCH₂, CH₂CH₂), 1.42-1.20 (m, 4H, CH₂CH₂), 1.03 (d, *J*=7.2 Hz, 3H, CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 207.1, 131.4, 131.1, 55.72, 42.4, 35.9, 33.3, 32.1, 30.5, 26.9, 26.8, 17.4; HRMS (CI) exact mass calcd for (C₁₂H₁₈O) requires *m/z* 178.1358, found *m/z* 178.1351; [α]_D = +168.0 (*c*=1.0, CHCl₃). Diastereomeric ratios were determined by ¹H NMR analysis. A portion of the title compound was converted to the (2*R*, 4*R*)-pentane-2,4-diol acetal for the determination of enantiomeric purity. 5.0 mg of the title compound was taken up in 1 mL of CH₂Cl₂. 4.0 mg of (2*R*, 4*R*)-pentane-2,4-diol and 0.5 mg of pTSA was added to the solution, and the reaction was stirred for 1 hour. NaHCO₃ solution (saturated) was then added, and the mixture was washed with EtOAc (2 x 5 mL). The combined organic extracts were washed with brine, dried over Na₂SO₄, and filtered. The resultant filtrate was loaded onto a short silica plug, eluted with EtOAc, and concentrated, to provide the acetal of the title compound: 90% ee (*endo*). Enantiomeric ratios were determined by GC with a Bodman β-DM column (23 psi, assay: hold 50 °C for 10 min, ramp 5 °C/min to 200 °C); *endo* isomers *t*_r = 38.7 min and 39.0.



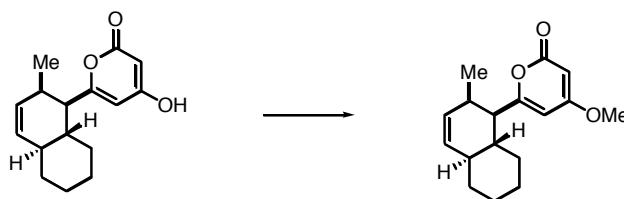
Methyl 5-hydroxy-5-[(1R,2R,4aR,8S,8aR)-1,2,4a,5,6,7,8,8a-octahydro-2-methylnaphthyl]-3-oxopentanoate 17. To a $-78\text{ }^{\circ}\text{C}$ solution of 143 mg (0.80 mmol) of aldehyde **16** in 15 mL of CH_2Cl_2 under nitrogen atmosphere was added a solution of methyl acetoacetate bis(trimethylsilyl)ether in 20 mL of CH_2Cl_2 . This solution was then treated with 800 μL (0.80 mmol) of TiCl_4 (1M in CH_2Cl_2) from a newly opened bottle. After stirring for 1 hour, the reaction was quenched with H_2O and extracted with CH_2Cl_2 (2 x 30 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 , filtered, and concentrated. Purification of the resultant residue by silica gel chromatography (20% EtOAc/hexanes) afforded 175 mg (75% yield) of the alcohol as a clear oil whose spectral characteristics matched those previously reported.



Methyl 4-[(1R,2R,4aR,8S,8aR)-1,2,4a,5,6,7,8,8a-octahydro-2-methylnaphthyl]-3,5-dioxobutanoate. To a solution of 175 mg (0.60 mmol) of alcohol in 6.0 mL of CH_2Cl_2 was added 254 mg (0.60 mmol) of Dess-Martin Periodinane. The solution was stirred at room temperature for 2 hours, after which 10 mL of 1:1 $\text{NaS}_2\text{O}_3/\text{NaHCO}_3$ aq. solution was added. The aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL), and the combined extracts were washed with brine. The organic extracts were dried over Na_2SO_4 , filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (10% EtOAc/hexanes) provided the β,γ -diketoester as a yellow oil in 71% yield (124 mg) whose spectral characteristics matched those previously reported.

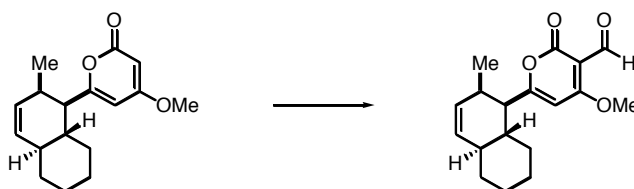


4-Hydroxy-6-[(1R,2R,4aR,8S,8aR)-1,2,4a,5,6,7,8,8a-octahydro-2-methylnaphthyl]-2H-pyran-2-one. To a solution of the β,γ -diketoester (67 mg, 0.23 mmol) in 2.5 mL of benzene was added DBU (67 μ L, 0.46 mmol), upon which the solution immediately turned bright yellow in color. The flask was sealed, and the solution was stirred at 60 °C for 3 hours. The reaction was then quenched with the addition of 1N HCl (0.8 mL) and extracted with EtOAc (2 x 10 mL). The combined organic extracts were then washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to afford the 4-hydroxypyrone as a bright yellow oil in 87% yield (58 mg) whose spectral characteristics matched those previously reported. **60** was taken on immediately to the next step without further purification.



4-Methoxy-6-[(1R,2R,4aR,8S,8aR)-1,2,4a,5,6,7,8,8a-octahydro-2-methylnaphthyl]-2H-pyran-2-one. A suspension of 4-hydroxypyrone (58 mg, 0.22 mmol), methyl *p*-toluenesulfonate (1.0 mmol), and potassium carbonate (1.0 mmol) in DMF (3 mL) was stirred at room temperature for 5 hours. The reaction was quenched with saturated NH₄Cl solution, and extracted with Et₂O (3 x 10 mL). The combined organic extracts were washed with brine, dried over Na₂SO₄ and filtered. Removal of volatiles under reduced pressure provided a yellow oily residue which was purified by silica gel flash chromatography (25% EtOAc/hexanes) to afford the 4-methoxypyrone as a yellow oil in 81% yield (49 mg): IR (film) 2927, 2858, 1722, 1645, 1568, 1452, 1413, 1251, 1159, 1159, 1035, 811; ¹H NMR (300 MHz, CDCl₃) δ 5.77 (d, *J*=2.4 Hz, 1H, CH=COC=O), 5.55 (ddd, *J*=2.7, 4.4, 10.5 Hz, 1H, CH=CHCH), 5.45-5.39 (m, 2H, CH=CHCH),

O=CCHCOMe), 3.79 (s, 3H, OCH₃), 2.62 (dd, *J*=6.0, 11.4 Hz, 1H, CHCOC=O), 2.44-2.41 (m, 1H, CHCH₃), 2.39-2.22 (m, 1H, CHCHCH₂), 1.81-1.52 (m, 5H, CHCH₂, CH₂CH₂), 0.94 (d, *J*=6.9 Hz, 3H, CHCH₃); ¹³C NMR (75 MHz, CDCl₃) δ 167.2, 165.2, 131.6, 131.4, 130.0, 101.9, 87.7, 56.1, 49.2, 43.4, 36.7, 35.4, 33.4, 30.4, 26.9, 26.8, 18.1; [α]_D = -101.7 (c=1, CHCl₃); HRMS (FAB+) exact mass calculated for [(C₁₇H₂₂O₃)H]⁺ requires *m/z* 275.1647, found *m/z* 275.1640.

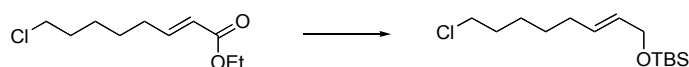


(-) **Solanapyrone D (18)**. To a -78 °C solution of diisopropyl amine (11.4 μL, 0.082 mmol) in 0.2 mL THF was added 28 μL (0.070 mmol) of nBuLi (2.5M in hexanes, freshly titrated). The solution was warmed to 0 °C and stirred for 20 minutes. The reaction was then cooled back to -78 °C, and 6.4 mg (0.023 mmol) of 4-methoxypyrene was added in THF (2 x 0.1 mL). The solution was stirred for an additional 20 minutes, after which methyl formate (28 μL, 0.46 mmol, freshly distilled) was added. After stirring for an additional 2.5 hours, the reaction was quenched with saturated NH₄Cl solution and extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The resultant crude yellow oily residue was purified by silica gel chromatography to afford Solanapyrone D as a yellow oil in 57% yield (3.9 mg, 91% yield based on recovered starting material): [α]_D = -201.1 (c=1, CHCl₃),): [α]_D literature¹⁷ = -148.7 (c=1, CHCl₃); IR (film) 2930, 2862, 1728, 1686, 1615, 1520, 1375, 1265 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 10.16 (s, 1H, CHO), 6.12 (s, 1H, CHC(OMe)=C(CHO)), 5.57 (ddd, *J*=2.7, 4.2, 9.9 Hz, 1H, CH=CHC(Me)H), 5.45 (d, *J*=9.9 Hz, 1H, CH=CHCH), 4.07 (s, 3H, OCH₃), 2.75 (dd, *J*=6.0, 11.0 Hz, 1H, CHC(Me)H), 2.50 (m, 1H, CHC(Me)H), 1.59-1.85 (m, 5H, CHCH₂, CH₂CH₂), 1.40-1.25 (m, 2H, CH₂CH₂), 1.21-1.11 (m, 1H, CHCH₂CH₂),

¹⁷ Hagiwara, H.; Kobayashi, K.; Miya, S.; Hoshi, T.; Suzuko, T.; Ando, M.; Okamoto, T.; Kobayashi, M.; Yamamoto, I.; Ohtsubo, S.; Kato, M.; Uda, H. *J. Org. Chem.* **2002**, 67, 5969.

0.99 (d, $J=7.5$, 3H, CHCH_3), 0.96-0.88 (m, 1H, CHCH_2CH_2); ^{13}C NMR (125 MHz, CDCl_3) δ 186.8, 176.3, 173.8, 162.2, 131.0, 130.7, 101.3, 96.0, 57.6, 50.8, 43.0, 36.5, 35.5, 30.2, 26.5, 26.3, 17.7; HRMS (FAB+) exact mass calcd for $[(\text{C}_{18}\text{H}_{22}\text{O}_4)\text{H}]^+$ requires m/z 303.1596, found m/z 303.1585.

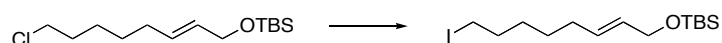
Preparation of 9-Methylene-11-phenyl-undeca-2,10-dien-1-ol (19).



A solution of 23.7 g (115.8 mmol) 8-Chloro-oct-2-enoic acid ethyl ester in 600 mL CH_2Cl_2 was cooled to -78°C . 45 mL (252.9 mmol) DIBAL-H was added slowly and the reaction was warmed to 25°C , quenched with MeOH (200 mL), and stirred with 300 mL Rochelle's salt solution (sat) for 8 hours. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 300 mL). The combined organic layers were washed with brine (200 mL), dried over Na_2SO_4 , and concentrated to afford 18.35 g (97%) of 8-Chloro-oct-2-en-1-ol as a clear oil with the following spectral data that was used with further purification: IR (film): 3328, 2933, 2857, 1461, 1309, 1089, 1002, 970, 731, 651 cm^{-1} ; ^1H NMR (300 MHz) δ 5.63 (m, 2H, $\text{C}_6\text{-H}$, $\text{C}_7\text{-H}$), 4.05 (d, $J = 4.8$ Hz, 2H, $\text{C}_8\text{-H}_2$), 3.50 (t, $J = 6.8$ Hz, 2H, $\text{C}_1\text{-H}_2\text{Cl}$), 2.03 (m, 2H, $\text{C}_5\text{-H}_2$), 1.75 (m, 2H, $\text{C}_2\text{-H}_2$), 1.45-1.34 (m, 4H, $\text{C}_3\text{-H}_2$, $\text{C}_4\text{-H}_2$); ^{13}C (300 MHz, CDCl_3) δ 132.8, 129.5, 63.9, 45.3, 32.8, 32.3, 28.7, 26.7.

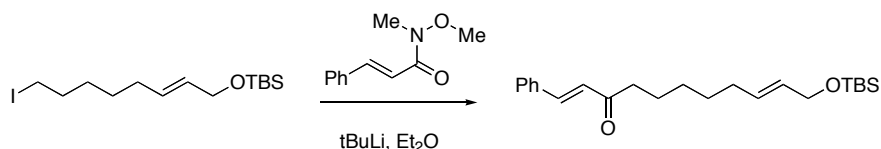
A solution of 460 mg (2.83 mmol) 8-Chloro-oct-2-en-1-ol, 0.8 mL (5.66 mmol) Et_3N , and 34 mg (2.83 mmol) DMAP in 3 mL CH_2Cl_2 was cooled to 0°C . 512 mg (3.39 mmol) of TBSCl was added and the reaction was warmed to room temperature and stirred for hrs. The reaction mixture was poured into 5 mL H_2O and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were washed with brine (15 mL), dried with Na_2SO_4 , filtered through cotton, and concentrated *in vacuo*. The resulting residue was flushed through a silica plug (10% EtOAc/ hexanes) to afford 773 mg (99%) of the TBS-protected alcohol as a clear oil:

IR (film) 2955, 2929, 2857, 1471, 1463, 1255, 1117, 1099, 1061, 970, 836, 776 cm^{-1} ; ^1H (300 MHz, CDCl_3) δ 5.69-5.50 (m, 2H, $\text{C}_6\text{-H}$, $\text{C}_7\text{-H}$), 4.13 (dd, $J = 4.9, 1.1$, 2H, C_8H_2), 3.54 (t, $J = 6.8$, 2H, $\text{C}_1\text{-H}_2$), 2.05 (dt, $J = 6.4$, 2H, $\text{C}_5\text{-H}_2$), 1.78 (m, 2H, $\text{C}_2\text{-H}_2$), 1.51-1.36 (m, 4H, $\text{C}_3\text{-H}_2$, $\text{C}_4\text{-H}_2$), 0.91 (s, 9H, $\text{SiC}(\text{CH}_3)_3$), 0.08 (s, 6H, $\text{Si}(\text{CH}_3)_2$); ^{13}C (300 MHz, CDCl_3) δ 131.1, 129.7, 64.3, 45.4, 32.8, 32.3, 28.8, 26.8, 26.4, 18.8, -4.7; LRMS (EI) m/z 219 (M- $t\text{Bu}$); HRMS (EI) exact mass calcd for $[(\text{C}_{14}\text{H}_{29}\text{ClOSi}) - t\text{Bu}^+]$ requires m/z 219.0972, found m/z 219.0968.



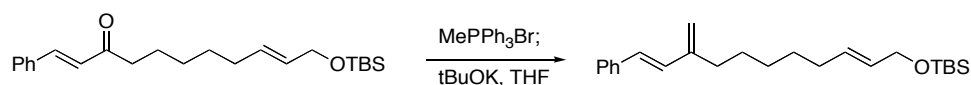
A solution of 62.4 g (225.3 mmol) of the alkyl chloride and 67.6 g (451.2 mmol) NaI in 220 mL acetone was stirred at reflux in the absence of light for 46 h. The reaction mixture was cooled to room temperature and poured into 100 mL of water. 150 mL of Et_2O was added and the layers were separated. The aqueous layer was extracted (3 x 100 mL) and the combined organics were dried with Na_2SO_4 , filtered through cotton, and concentrated *in vacuo*. The resulting residue was flushed through a silica plug (10% EtOAc / hexanes) to afford 68.1 g (82%) of the alkyl iodide as a pale, yellow oil:

IR (film) 2955, 2928, 2856, 1472, 1462, 1255, 1105, 1059, 969, 836, 776 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.68-5.50 (m, 2H, $\text{C}_6\text{-H}$, $\text{C}_7\text{-H}$), 4.13 (dd, $J = 4.9, 0.8$ Hz, 2H, $\text{C}_8\text{-H}_2$), 3.19 (t, $J = 7.2$ Hz, 2H, $\text{C}_1\text{-H}_2$), 2.05 (m, 2H, $\text{C}_5\text{-H}_2$), 1.88-1.79 (m, 2H, C_2H_2), 1.44-1.38 (m, 4H, C_3H_2 , C_4H_2), 0.91 (s, 9H, $\text{SiC}(\text{CH}_3)_3$), 0.08 (s, 6H, $\text{Si}(\text{CH}_3)_2$); ^{13}C NMR (300 MHz, CDCl_3) δ 130.9, 129.6, 64.2, 33.7, 32.2, 30.3, 28.4, 26.3, 18.8, 7.4, -4.7; LRMS (EI) m/z 311 (M- $t\text{Bu}$); HRMS (EI) exact mass calcd for $[(\text{C}_{14}\text{H}_{29}\text{IOSi}) - t\text{Bu}^+]$ requires m/z 311.0328, found m/z 311.0332.



To a solution of 10.0 g (27.1 mmol) of the alkyl iodide in 170 mL Et_2O at -78°C was added 35.39 mL (60.16 mmol) of $t\text{-BuLi}$ (1.7 M in pentane). The solution was stirred for

30 minutes at $-78\text{ }^{\circ}\text{C}$, upon which 10.4 g (54.3 mmol) amide¹⁸ was added in 20 mL Et_2O . The solution was warmed to $25\text{ }^{\circ}\text{C}$ after 10 minutes and stirred for an additional 1 hour. The reaction mixture was poured into 150 mL of 1N NH_4Cl . The layers were separated and the aqueous layer was extracted with Et_2O (3 x 100 mL). The organic layers were combined, washed with brine (200 mL), dried with Na_2SO_4 , filtered through cotton, and concentrated *in vacuo*. Purification of the resulting residue by flash chromatography (gradient, 2.5-5% EtOAc / hexanes) afforded 3.47 g (35%) of the ketone as a yellow oil: IR (film) 2929, 2856, 1691, 1668, 1255, 1100, 1055, 972, 836, 776 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.57-7.52 (m, 3H, PhH , $\text{C}_{11}\text{-H}$), 7.40-7.37 (m, 2H, PhH), 6.74 (d, $J = 16.2$ Hz, 1H, $\text{C}_{10}\text{-H}$), 5.69-5.49 (m, 2H, $\text{C}_2\text{-H}$, $\text{C}_3\text{-H}$), 4.12 (dd, $J = 4.9, 1.1$ Hz, 2H, $\text{C}_1\text{-H}_2$), 2.66 (t, $J = 7.6$ Hz, 2H, $\text{C}_8\text{-H}_2$), 2.05 (dt, $J = 6.6$ Hz, 2H, $\text{C}_4\text{-H}_2$), 1.68 (tt, $J = 7.4$ Hz, 2H, $\text{C}_7\text{-H}_2$), 1.39 (m, 4H, $\text{C}_6\text{-H}_2$, $\text{C}_5\text{-H}_2$), 0.91 (s, 9H, $\text{SiC}(\text{CH}_3)_3$), 0.07 (s, 6H, $\text{Si}(\text{CH}_3)_2$); ^{13}C NMR (300 MHz, CDCl_3) δ 200.4, 142.3, 134.6, 131.2, 130.4, 129.3, 129.0, 128.3, 126.2, 64.2, 41.1, 32.2, 29.2, 29.1, 26.2, 24.4, 18.7, -4.8; LRMS (EI) m/z 315(M- $t\text{Bu}$); HRMS (EI) exact mass calcd for $[(\text{C}_{23}\text{H}_{36}\text{O}_2\text{Si}) - t\text{Bu}^+]$ requires m/z 315.1780, found m/z 315.1783.

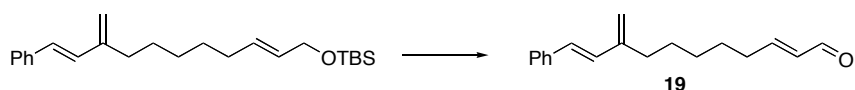


To a solution of 108 mg (0.97 mmol) of $t\text{BuOK}$ in 10 mL THF was added 345 mg (0.97 mmol) of MePPh_3Br . The yellow solution was stirred at room temperature for 1 h, then cooled to $0\text{ }^{\circ}\text{C}$, and 300 mg (0.81 mmol) of the ketone was added in 4 mL THF. The solution was warmed to room temperature and stirred for an additional 1 hour, then poured into 10 mL of water. 15 mL of Et_2O were added and the layers were separated. The aqueous layer was extracted with Et_2O (3 x 15 mL). The combined organics were dried with Na_2SO_4 , filtered through cotton, and concentrated *in vacuo*. Purification of the resulting residue by flash chromatography (2.5 % EtOAc / hexanes) afforded 218 mg (61%) of the triene as a cloudy oil:

IR (film) 2929, 2856, 1641, 1255, 1098, 1057, 1098, 1057, 962, 836, 776, 753, 694 cm^{-1} ;

¹⁸ *Euro. J. Org. Chem.* **1999**, 2309-2914.

^1H NMR (300 MHz, CDCl_3) δ 7.48-7.22 (m, 5H, PhH), 6.84 (d, $J = 16.2$ Hz, 1H, $\text{C}_{11}\text{-H}$), 6.61 (d, $J = 16.5$ Hz, 1H, $\text{C}_{10}\text{-H}$), 5.74-5.54 (m, 2H, $\text{C}_2\text{-H}$, $\text{C}_3\text{-H}$), 5.17 (s, 1H, $\text{C}=\text{CHH}$), 5.09 (s, 1H, $\text{C}=\text{CHH}$), 4.17 (dd, $J = 5.1, 1.0$ Hz, 2H, $\text{C}_1\text{-H}_2$), 2.36 (t, $J = 7.1$ Hz, 2H, $\text{C}_8\text{-H}_2$), 2.09 (dt, $J = 6.4$ Hz, 2H, $\text{C}_4\text{-H}_2$), 1.65-1.55 (m, 2H, $\text{C}_7\text{-H}_2$), 1.49-1.37 (m, 4H, $\text{C}_5\text{-H}_2$, $\text{C}_6\text{-H}_2$), 0.96 (s, 9H, $\text{SiC}(\text{CH}_3)_3$), 0.12 (s, 6H, $\text{Si}(\text{CH}_3)_2$); ^{13}C NMR (300 MHz, CDCl_3) δ 146.3, 137.5, 131.4, 131.2, 129.3, 128.7, 128.0, 127.4, 126.5, 116.3, 64.3, 32.4, 32.2, 29.4, 29.3, 28.4, 26.3, 18.7, -4.7; LRMS (EI) m/z 313(M- $t\text{Bu}$); HRMS (EI) exact mass calcd for $[(\text{C}_{24}\text{H}_{38}\text{OSi}) - t\text{Bu}^+]$ requires m/z 313.1988, found m/z 313.1981.



To a stirred solution of 1.34 g (3.62 mmol) of the triene in 7.2 mL THF at 0°C was added 2.36 g (9.03 mmol) of $\text{TBAF}\cdot\text{H}_2\text{O}$. After 10 minutes, the ice bath was removed the reaction was stirred at room temperature for an additional 40 minutes, then 15 mL H_2O was added and the resulting solution was extracted with Et_2O (3 x 10 mL). The combined organics were washed with brine (15 mL), dried over Na_2SO_4 , filtered through cotton, and concentrated *in vacuo*. Purification of the residue by flash chromatography (20% EtOAc / hexanes) afforded 800 mg (86%) of 9-Methylene-11-phenyl-undeca-2,10-dien-1-ol as a clear oil:

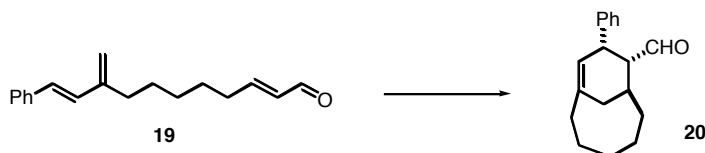
IR (film) 3025, 2929, 2856, 1602, 1448, 963, 886, 754, 694 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.45-7.2 (m, 5H, PhH), 6.81 (d, $J = 16.5$ Hz, 1H, $\text{C}_{11}\text{-H}$), 6.57 (d, $J = 16.5$ Hz, 1H, $\text{C}_{10}\text{-H}$), 5.76-5.59 (m, 2H, $\text{C}_2\text{-H}$, $\text{C}_3\text{-H}$), 5.14 (s, 1H, $\text{C}=\text{CHH}$), 5.06 (s, 1H, $\text{C}=\text{CHH}$), 4.09 (m, 2H, $\text{C}_1\text{-H}_2$), 2.32 (t, $J = 7.7$, 2H, $\text{C}_8\text{-H}_2$), 2.07 (dt, $J = 6.9$, 2H, $\text{C}_1\text{-H}_2$), 1.56 (m, 2H, $\text{C}_7\text{-H}_2$), 1.46-1.37 (m, 4H, $\text{C}_5\text{-H}_2$, $\text{C}_6\text{-H}_2$); ^{13}C NMR (300 MHz, CDCl_3) δ 146.3, 137.5, 133.5, 131.2, 129.0, 128.7, 128.0, 127.5, 126.5, 116.3, 64.1, 32.5, 32.2, 29.4, 29.3, 28.4; LRMS (EI) m/z 256; HRMS (EI) exact mass calcd for $[(\text{C}_{18}\text{H}_{24}\text{O})]$ requires m/z 256.1827, found m/z 313.1981.

To a solution of 800 mg (3.12 mmol) of the free alcohol in 6 mL CH_2Cl_2 was added 731 mg (6.24 mmol) N-methylmorpholine-N-oxide and 80 mg 4A molecular sieves. After 15 minutes, 55 mg (0.16 mmol) of tetrapropylammonium perruthenate was added. After 15

minutes more, the crude reaction mixture was flushed through a 3" silica plug with Et₂O (200 mL) and the eluent was concentrated to afford 760 mg (96%) of **19** as a pale yellow oil:

IR (film) 3025, 2932, 2858, 1690, 1639, 1602, 1494, 1448, 1157, 1120, 966, 886, 754, 697 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 9.51 (dd, *J* = 2.5, 8.0, 1H, C₁-H), 7.45-7.20 (m, 5H, Ph-H), 6.91-6.80 (m, 1H, C₃-H), 6.81 (d, *J* = 16.2, 1H, C₁₁-H), 6.58 (d, *J* = 16.5, 1H, C₁₀-H), 6.18-6.08 (m, 1H, C₂-H), 5.15 (s, 1H, C=CHH), 5.06 (s, 1H, C=CHH), 2.39-2.32 (m, 2H, C₄-H₂), 2.34 (t, *J* = 7.1, 2H, C₈-H₂), 1.64-1.51 (m, 4H, C₇-H₂, C₅-H₂), 1.48-1.37 (m, 2H, C₆-H₂); ¹³C NMR (300 MHz, CDCl₃) δ 194.1, 158.9, 146.0, 137.4, 133.1, 131.0, 128.7, 128.0, 127.5, 126.5, 116.4, 33.0, 32.1, 29.3, 28.2, 28.0; LRMS (EI) *m/z* 254; HRMS (EI) exact mass calcd for [(C₁₈H₂₂O)] requires *m/z* 254.1671, found *m/z* 254.1668.

IMDA Reaction of **19**.



(8*R*, 9*S*)-9-phenylbicyclo[5.3.1]undec-1-(10)-ene-8-carbaldehyde (20). A solution of 3.9 mg (0.016 mmol) of **2** and 3.0 mg (0.016 mmol) of pTSA•H₂O in 0.4mL of CHCl₃ (2% H₂O) was added to 20 mg (0.079 mmol) of **19** at room temperature. After 41 hrs, flash chromatography (5% EtOAc/hexanes) afforded 13 mg (65%) of **20** followed by 2 mg (10%) of **19** (72% yield of **20** based on 90% conversion). GC analysis of **20** showed that it was formed in 98.4% *ee* (Chiral β-DA, 90° isotherm for 20 minutes, then ramp 20°/minute to 180°; *t_r* (minor) 29.2, *t_r* (major) 29.6) and was a >99:1 mixture of isomers. [<α]_D²⁵ +75.1° (*c* = 1.0, CHCl₃); IR (film) 2923, 2854, 1722, 1453, 1260, 1021, 775, 699 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 9.66 (d, *J* = 1.6 Hz, 1H, CHO), 7.34-7.19 (m, 5H, PhH), 5.62 (br, C₂-H), 3.66 (m, 1H, C₃-H), 2.46 (m, 1H, C₄-H), 2.33 (m, 1H, C₆-HH), 2.29 (m, 1H, C₆-HH), 2.21-2.12 (m, 3H), 1.92-0.82 (m, 8H); ¹³C NMR (300 MHz, CDCl₃) δ 202.7, 145.7, 140.4, 128.9, 128.4, 126.6, 126.4, 62.1, 40.4, 36.1, 35.7, 33.0,

29.6, 29.5, 28.9, 25.4; LRMS (EI) m/z 254; HRMS (EI) exact mass calcd for $[(C_{18}H_{22}O)]$ requires m/z 254.1671, found m/z 254.1673.